

REMARKS

I. Introduction

Applicants acknowledge receipt of the September 9, 2010 Office Action. In the Action, Examiner Horning objected to: (1) the specification for containing embedded hyperlink and uncapitalized trademarks; and (2) claims 85, 109 and 116 for informalities.

The Examiner rejected claims 109-113 as allegedly being anticipated by WO 02/36792 ("Catchpole"), as well as claim 124 as allegedly being anticipated by Li et al. (*Gene Therapy*, 2001) as further evidenced by Moriarty et al. (*PNAS*, 1981) and Dean et al. (*Expt. Cell Res.*, 1999).

The Examiner further rejected the following claims for allegedly being obvious:

(1) claims 125-128 over Li et al. (*Gene Therapy*, 2001) in view of Catchpole as further evidenced by Moriarty and Dean.

(2) claims 85-93, 96-102 and 116 over the combination of Catchpole, Thudium (WO 02/031137), Li, Ivy (USP 6,165,477), and Palmiter (*PNAS*, 1991) as further evidenced by Moriarty, Dean, Asselbergs (U.S. Publ. No. 2003/0124523) and Renner (U.S. Publ. No. 2003/0175711).

(3) claim 103 over the combination of Catchpole, Thudium, Li, Ivy, Palmiter and in further view of Scharton-Kersten (*Infection and Immunity*, 2000) as further evidenced by Moriarty, Dean, Asselbergs and Renner.

Additionally, the Examiner issued a provisional double patenting rejection against claims 85-93, 96-103, 109-113, 116, 124-128 as being unpatentable over claims 115-123, 126, 132-133, 137-156 of copending U.S. Application No. 11/815, 278.

Applicants respectfully request reconsideration of the present application in view of the forgoing amendments and in view of the reasons that follow.

II. Status of Claims

Claims 1-84 are canceled. Claims 94, 95, 104-108, 114, 115, 117-123, 129 and 130 are withdrawn. Claim 85, 109 and 116 are presently amended. Support for the amendments to independent claims 85, 109 and 116 may be found, for instance, in paragraphs [0153] and [0166] and Figure 12 of Applicant's published application (Pub. No. U.S. 2008/0160048). Claims 85-93, 96-103, 109-113, 116 and 124-128 are currently pending and under review.

Applicant notes that withdrawn claims 94-95 and 117-121 correspond to elected Group I (with traverse), drawn to a nucleic acid construct. The Examiner has withdrawn these claims from consideration based on the species election as required by the Examiner. Office Action, page 1. As noted in Applicant's Response to the Restriction Requirement dated April 26, 2010, once the elected species is found patentable, the Examiner should consider the full scope of claims in Group I, including claims 94-95 and 117-121.

III. Objections to Specification

The Examiner objects to the specification for containing an embedded hyperlink. Applicants have amended the specification to delete the embedded hyperlink.

The Examiner further objects to the specification for failing to capitalize the trademark POWDERJECT. Applicants have amended the specification to change "the PowderJect® needleless syringe device" to "the POWDERJECT® needleless syringe device," as recommended by the Examiner.

Applicants therefore respectfully request that there objections be withdrawn.

IV. Claim Objections

The Examiner objects to claims 85, 109 and 116 for reciting "a hCMV" instead of "an hCMV". Applicants have amended claims 85, 109 and 116 to recite "an hCMV" as

recommended by the Examiner, and thereby respectfully request that these objections be withdrawn.

V. Claim Rejections under 35 USC § 102

Claims 109-113 stand rejected as allegedly being anticipated by Catchpole. Applicants respectfully traverse.

The Examiner states that Catchpole describes vectors that include “exon 1 and a heterologous intron that replaces the natural intron A of HCMV IE1.” *See* Office Action, page 4, last paragraph (citing page 2, lines 1-8, in Catchpole). The Examiner also asserts that Catchpole “describes including a part of HCMV IE1 exon 2.” *Id.* (citing page 4, lines 3-10, in Catchpole).

Catchpole’s teaching differs from the present invention, at minimum with regard to the placement of the heterologous intron in relation to exon 1 and exon 2. Specifically, Catchpole discloses placing the heterologous intron either “*immediately downstream* of exon 1” and/or that “the untranslated part of [] exon 2 may be included *immediately downstream* of the heterologous intron” (page 4, lines 3-10) (emphasis added). In other words, at best, Catchpole suggests the concept of placing a heterologous intron in the middle of exons 1 and 2, and therefore placing the heterologous intron upstream (i.e., 5’) to “the untranslated part of [] exon 2” present in a vector. Thus, at most, Catchpole discloses a vector comprising (5’ → 3’) *exon 1, heterologous intron, and exon 2*.

By contrast, as disclosed by Applicant for the first time, “the present chimeric construct ... is ... without intervening intron sequence [in exon sequence (b)].” *See* Paragraph [0153] of Applicant’s published application; *see also* Figure 12 in specification. Exon sequence (b) corresponds to “exon 1 and at least a part of exon 2 of the hCMV major immediate early gene.” *See id.* at paragraphs [0136]-[0139]. To expedite prosecution of this application without acquiescing to the Examiner’s rejection, Applicant has amended claim 109 (and claims 85 and 116) to recite “wherein the heterologous intron is not positioned between the exon 1 and the at

least a part of exon 2 in (b)” Claim 109 (and claims 85 and 116) as amended therefore differs from Catchpole, which discloses a vector with a heterologous intron positioned between exons 1 and 2.

Nothing in Catchpole teaches, nor even suggests, the concept of placing a heterologous intron in a position other than between exon 1 and exon 2. Rather, it discloses a vector having the heterologous intron “immediately downstream of exon 1” and exon 2 “immediately downstream of the ... intron” (page 4, line 5-6 and 9-10, respectively). In other words, Catchpole discloses a vector with a heterologous intron between exon 1 and exon 2, i.e., discloses placing the heterologous intron as a substitution in the exact same position where intron A would normally exist in the HCMV IE1 gene. Nothing in Catchpole discloses or suggests inserting the heterologous intron elsewhere.

Applicants therefore respectfully request that the anticipation rejection of claims 109-113 based on Catchpole be withdrawn.

Claim 124 stands rejected as allegedly being anticipated by Li as further evidenced by Moriarty and Dean. Applicants respectfully traverse.

The Examiner states that Li describes a nucleic acid construct comprising a promoter sequence, a coding sequence and a 72 bp simian virus 40 (SV40) enhancer and thereby allegedly anticipates claim 124 of the present invention. Office Action, page 5, 4th paragraph. Applicants would like to point out, however, that claim 124 recites an enhancer “derived from ... a 3'UTR of a *simian CMV* immediate early gene sequence” (emphasis added). As disclosed in paragraph [0005] of Applicant’s published application, CMV stands for cytomegalovirus. Cytomegalovirus (CMV) and simian virus 40 (SV40) are two different viruses. Enhancers derived from SV40 therefore differ from enhancers derived from CMV. In fact, Li itself expressly teaches that enhancers from these two different viruses behave differently. For example, as noted in the abstract of Li, low levels of gene expression using CMV enhancers

“have limited the use of muscle as a target tissue,” while the use of the SV40 enhancer increases gene expression in this tissue. In addition, as taught in Li:

Simian virus 40 (SV40) enhancer has been demonstrated to exhibit transcriptional activity and, more important, to facilitate nuclear transport of plasmids from cytoplasm *in vitro*. ... In these previous studies, *only the SV40 viral enhancer increased nuclear uptake of plasmid, whereas the CMV ... enhancers do not.*”

Li, page 494, 2nd col., 2nd paragraph (citations omitted) (emphasis added).

In short, Li does not disclose nor suggest using an enhancer “derived from ... a 3'UTR of a simian CMV immediate early gene sequence,” but rather teaches the use of a different enhancer, i.e., an SV40 enhancer. Thus, Li fails to teach at least one element of claim 124, i.e., an enhancer “derived from ... a 3'UTR of a simian CMV immediate early gene sequence.”

When asserting anticipation by Li, the Examiner also states that “Moriarty et al. is cited for using a SV40 which comprises the SV40 enhancer homologous to that of SEQ ID NO: 8.” Applicant respectfully disagrees. Moriarty teaches the expression of hepatitis B virus surface antigen gene using a SV40 vector. Moriarty does not mention using an SV40 enhancer (nor any enhancer at all). Furthermore, the Examiner has provided no evidence or citation (and Applicant knows of none) indicating that SEQ ID NO: 8 is homologous to any part of the SV40 virus sequence.

Applicants therefore respectfully request that the anticipation rejection of claim 124 based on Li be withdrawn.

VI. Claim Rejections under 35 USC § 103

The Examiner has issued three obviousness rejections:

(1) Claims 125-128 stand rejected for allegedly being obvious over Li in view of Catchpole as further evidenced by Moriarty and Dean.

Claims 125-128 depend from claim 124. As discussed above in section V, Li does not teach at least one element of claim 124, i.e., an enhancer derived from a 3'UTR of a simian CMV immediate early gene sequence ("the CMV enhancer element"). In fact, Li appears to teach away from using a CMV enhancer when disclosing that "only the SV40 viral enhancer increased nuclear uptake of plasmid [in various cell types in culture], whereas the CMV and [RSV] enhancers do not." Li, page 494, 2nd col., 2nd paragraph.

Because none of the other three references (Catchpole, Moriarty and Dean) mention the use of a CMV enhancer, all four cited references, either alone or in combination, fail to teach or suggest the CMV enhancer element of the present invention. Applicants therefore respectfully request that this obviousness rejection be withdrawn.

(2) Claims 85-93,96-102 and 116 stand rejected for allegedly being obvious over the combination of Catchpole, Thudium, Li, Ivy, and Palmiter as further evidenced by Moriarty, Dean, Asselbergs and Renner.

As discussed above in section V, Catchpole does not teach at least one element recited in claims 85, 109 and 116 as amended, i.e., "wherein the heterologous intron is not positioned between the exon 1 and the at least a part of exon 2 in (b)" ("the intron-not-between element"). Because none of the other eight references (Thudium, Li, Ivy, Palmiter, Moriarty, Dean, Asselbergs and Renner) teach or suggest the intron-not-between element as recited in claims 85, 109 and 116, the nine references combined do not teach or suggest this element. Specifically, as discussed above, nothing in Catchpole discloses, nor suggests, the concept of placing a heterologous intron in a position other than between exon 1 and exon 2. Rather, it teaches a vector having the heterologous intron "immediately downstream of exon 1" and exon 2 "immediately downstream of the ...intron" (page 4, line 5-6 and 9-10, respectively). Catchpole discloses placing the heterologous intron in the same position where intron A would normally exist in the HCMV IE1 gene, i.e., between exon 1 and exon 2. Nothing in Catchpole suggests inserting the heterologous intron anywhere else in a construct, nor any rationale for doing so. Nothing in any of the other cited references overcome or otherwise point to this deficiency in

Catchpole. Applicants therefore respectfully request that this obviousness rejection be withdrawn.

(3) Claim 103 stands rejected over the combination of Catchpole, Thudium, Li, Ivy, Palmiter and in further view of Scharton-Kersten as further evidenced by Moriarty, Dean, Asselbergs and Renner.

Claim 103 depends from claim 85 via claims 102 and 101. As discussed above, Catchpole does not teach or suggest at least one element recited in claim 85, i.e., “wherein the heterologous intron is not positioned between the exon 1 and the at least a part of exon 2 in (b)” (“the intron-not-between element”). Nothing in any of the other cited references suggest, overcome or otherwise point to this deficiency in Catchpole. Because none of the other nine references (Thudium, Li, Ivy, Palmiter, Scharton-Kersten, Moriarty, Dean, Asselbergs and Renner) teach or suggest the intron-not-between element of the present invention, the ten references combined cannot teach or suggest this element. Applicants therefore respectfully request that this obviousness rejection be withdrawn.

VII. Double Patenting Rejection

The Examiner provisionally rejects claims 85-93, 96-103, 109-113, 116, 124-128 as being unpatentable over claims 115-123, 126, 132-133, 137-156 of copending Application No. 11/815, 278. Applicants respectfully request that the Office hold the provisional double-patenting rejection in abeyance pending indications of allowable subject matter in the current and other pending application, at which time the Applicants respectfully request that the Office contact the undersigned to discuss options to overcome the rejection.

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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